Claims:

1. A method of identifying a subject predisposed to lacunar stroke, the method including the step of identifying in the subject the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus.

2. A method according to claim 1, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

3. A method according to claims 1 or 2, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

4. A method of identifying a subject predisposed to small vessel occlusion, the method including the step of identifying in the subject the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus.

5. A method according to claim 4, wherein the small vessel occlusion manifests clinically as a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease including ischemic cardiomyopathy, peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy including small and large bowel ischemia, diffuse pulmonary embolism, and vascular impotence.

6. A method according to claims 4 or 5, wherein the small vessel occlusion occurs in the brain.

7. A method according to any one of claims 4 to 6, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

8. A method according to any one of claims 4 to 7, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

9. A method of identifying a subject predisposed to developing a disease or condition associated with small vessel occlusion, the method including the step of identifying in the subject the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase locus.

10. A method according to claim 9, wherein the disease or condition is a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

11. A method according to claims 9 or 10, wherein the disease or condition is associated with a small vessel occlusion in the brain.

12. A method according to any one of claims 9 to 11, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

13. A method according to any one of claims 9 to 12, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

14. A method of determining the risk of lacunar stroke in a subject, the method including the step of determining the presence of a thymine to cytosine mutation at position –107 in one or both alleles of the paraoxonase 1 locus.

15. A method according to claim 14, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject suffering a lacunar stroke, as compared to the risk of lacunar stroke for a subject in the general population.

16. A method according to claim 14, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject suffering a lacunar stroke, as compared to the risk of lacunar stroke for a subject with similar other risk factors for lacunar stroke.

17. A method according to any one of claims 14 to 16, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

18. A method according to any one of claims 14 to 17, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

19. A method of determining the risk of small vessel occlusion in a subject, the method including the step of determining the presence of a thymine to cytosine mutation at position –107 in one or both alleles of the paraoxonase 1 locus.

20. A method according to claim 19, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject suffering a small vessel occlusion, as compared to the risk of a small vessel occlusion for a subject in the general population.

21. A method according to claim 19, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject suffering a small vessel occlusion, as

compared to the risk of a small vessel occlusion for a subject with similar other risk factors for a small vessel occlusion.

22. A method according to any one of claims 19 to 21, wherein the small vessel occlusion manifests clinically as a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease including ischemic cardiomyopathy, peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy including small and large bowel ischemia, diffuse pulmonary embolism, and vascular impotence.

23. A method according to any one of claims 19 to 22, wherein the small vessel occlusion occurs in the brain.

24. A method according to any one of claims 19 to 23, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

25. A method according to any one of claims 19 to 24, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

26. A method of determining the risk of developing a disease or condition associated with small vessel occlusion in a subject, the method including the step of determining the presence of a thymine to cytosine mutation at position –107 in one or both alleles of the paraoxonase 1 locus.

27. A method according to claim 26, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject developing a disease or condition associated with small vessel occlusion, as compared to the risk of developing a disease or condition for a subject in the general population.

28. A method according to claim 26, wherein the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus indicates an increased risk of the subject suffering a lacunar stroke, as compared to the risk of a small vessel occlusion lacunar for a subject with similar other risk factors for a small vessel occlusion.

29. A method according to any one of claims 26 to 28, wherein the disease or condition is a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease including ischemic cardiomyopathy, peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy including small and large bowel ischemia, diffuse pulmonary embolism, or vascular impotence.

30. A method according to any one of claims 26 to 28, wherein the disease or condition is disease or condition associated with small vessel occlusion in the brain.

31. A method according to any one of claims 26 to 30, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

32. A method according to any one of claims 26 to 31, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

33. A method of identifying a subject suitable for treatment with an agent that decreases the activity of paraoxonase 1, the method including the step of determining in the subject the presence of a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus.

34. A method according to claim 33, wherein the subject has an increased risk of suffering a lacunar stroke, an increased risk of suffering a small vessel occlusion, including a small vessel occlusion in the brain, or an increased risk of

developing a disease or condition associated with small vessel occlusion, including a disease or condition associated with small vessel occlusion in the brain.

35. A method according to claim 34, wherein the disease or condition is a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease including ischemic cardiomyopathy, peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy including small and large bowel ischemia, diffuse pulmonary embolism, or vascular impotence.

36. A method according to any one of claims 33 to 35, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

37. A method according to any one of claims 33 to 36, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

38. A method of treating a subject susceptible to suffering a lacunar stroke, the method including the step of administering to the subject an effective amount of an agent that decreases the activity of paraoxonase 1.

39. A method of treating a subject susceptible to a small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the step of administering to the subject an effective amount of an agent that decreases the activity of paraoxonase 1.

40. A method according to claim 39, wherein the small vessel occlusion is a small vessel occlusion in the brain, including a small vessel occlusion manifesting clinically as a lacunar stroke.

41. A method according to claim 39, wherein the disease or condition is a lacunar stroke, cerebral leukoaraiosis, dementia, ischemic heart disease including ischemic cardiomyopathy, peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy including small and large bowel ischemia, diffuse pulmonary embolism, or vascular impotence.

42. A method of identifying an agent for treating a subject susceptible to lacunar stroke, small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the steps of:

(a) exposing an agent to a cell expressing PON1, wherein the cell includes a mutation that results in overexpression of PON1 compared to a cell without the mutation;

(b) determining the level of expression and/or activity of PON1 from the cell; and

(c) identifying the agent as an agent capable of decreasing the expression and/or activity of PON1.

43. A method according to claim 42, wherein the mutation is a thymine to cytosine mutation at position –107 in the paraoxonase 1 locus.

44. A method according to claims 42 or 43, wherein the cells includes a thymine to cytosine mutation at position –107 in both alleles of the paraoxonase 1 locus.

45. An agent identified according to the method of any one of claims 42 to 44.

46. A method of identifying an agent for treating a subject susceptible to a lacunar stroke, small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the steps of:

(a) exposing an agent to a cell transformed with all or part of the PON1 locus, wherein the transformed locus includes a thymine to cytosine

mutation at position –107 and the transformed locus regulates expression of a reporter gene;

(b) determining the level of expression of the reporter gene in the cell so exposed to the agent; and

(c) identifying the agent as an agent that decreases PON1 expression by the decrease in expression of the reporter gene.

47. An agent identified according to the method of claim 46.

48. An isolated nucleic acid consisting of the sequence according to SEQ. ID No.3 or RNA equivalent thereof.

49. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 3, wherein the nucleic acid hybridises with the complement of SEQ ID No. 3 under stringent hybridisation conditions and the stringent hybridisation conditions include hybridisation in 6xSSC at 42°C and washing in 2xSSC at 20°C.

50. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 3, wherein the nucleic acid has at least 80% homology to SEQ. ID No.3 or RNA equivalent thereof.

51. An isolated nucleic acid consisting of the sequence according to SEQ. ID No.4 or RNA equivalent thereof.

52. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 4, wherein the nucleic acid hybridises with the complement of SEQ ID No. 4 under stringent hybridisation conditions and the stringent hybridisation conditions include hybridisation in 6xSSC at 42°C and washing in 2xSSC at 20°C.

53. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 4, wherein the nucleic acid has at least 80% homology to SEQ. ID No.e or RNA equivalent thereof.

54. An isolated nucleic acid consisting of the sequence according to SEQ. ID No.5 or RNA equivalent thereof.

55. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 5, wherein the nucleic acid hybridises with the complement of SEQ ID No. 5 under stringent hybridisation conditions and the stringent hybridisation conditions include hybridisation in 6xSSC at 42°C and washing in 2xSSC at 20°C.

56. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 5, wherein the nucleic acid has at least 80% homology to SEQ. ID No.5 or RNA equivalent thereof.